

Comparison of community-acquired and nosocomial legionella pneumonia cases in Konya, Turkey

Legionella pneumonia

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Abstract

Aim: Legionella pneumophila is an important cause of community and hospital-acquired pneumonia. The aim of this study was to compare the clinical findings, risk factors, and laboratory and radiological data of 20 nosocomial and 26 community-acquired cases with the diagnosis of L. pneumophila pneumonia between April 2017 and October 2019 retrospectively.

Material and Methods: Twenty patients with nosocomially acquired Legionella pneumonia (NALP), and twenty-six patients with community-acquired Legionella pneumonia (CALP) were included in the study. We applied the Centers for Disease Control (CDC) and World Health Organization (WHO) criteria for the diagnosis both of nosocomial infection and Legionella pneumonia. The diagnosis was based on the positivity of urinary antigen test for Legionella pneumonia (Acro Biotech, USA). Statistical analysis was performed using chi-square and independent student t-test using SPSS Statistics 25.0 program.

Results: Among the risk factors, older age was more common in the NALP group than in the CALP group, whilst chronic lung disease and cancer were more common in the NALP group than in the CALP group. The radiological features at presentation and during the evolution were similar in both groups. While CRP level was found to be high in the CALP group, ALT, AST, total and direct bilirubin levels, prothrombin time and INR values were significantly higher in the NALP group. Statistical analysis showed that myalgia was more common in the CALP group than in the NALP group. When both groups were compared in terms of mortality rates and SOFA and APACHE scores, no statistically significant difference was detected.

Discussion: As a result of our study, radiological and laboratory findings of the cases with community-acquired and nosocomial Legionella pneumonia in our region were found to be similar to previous studies.

Keywords

Legionella, Pneumonia, Nosocomial

Introduction

Legionella is a facultative, intracellular bacterium that penetrates and proliferates in the phagosomes of alveolar macrophages and serum monocytes [1]. Legionella pneumophila is one of the causative agents of hospital-acquired pneumonia, which can progress from a mild clinical picture to severe multiple organ failure and show a wide clinical spectrum in the population. It can cause epidemics, especially by colonizing water systems and being transmitted via aerosol in environments such as hotels and hospitals [2]. Legionella pneumophila is an important cause of community-acquired and hospital-acquired pneumonia. This infection, which can have both social and nosocomial origins, was first detected in 1976 [3]. Legionella Disease (LD), which is still often referred to as lung infections that present with different symptoms, is characterized by interstitial patterns on chest X-ray and typical bacteria (e.g., Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus) [4, 5].

Although LD is transmitted from the environment through inhalation of aerosol containing the bacteria, outbreaks occur more frequently in sporadic form. Person-to-person transmission does not occur [2]. It is reported that the frequency of LD in community-acquired pneumonia requiring hospitalization in adults varies between 5-10% [2]. Diagnosis cannot be made easily due to nonspecific clinical findings, radiological features and the need for special laboratory tests. The most specific tests for diagnosis are the detection of Legionella antigen in culture and urine [6].

In this study, we aimed to compare the risk factors, clinical findings, and laboratory and radiological imaging findings in community-acquired and hospital-acquired Legionella pneumonia cases that we diagnosed and hospitalized in our hospital.

Material and Methods

This study was carried out at Başkent University Konya Application and Research Hospital between April 2017 and October 2019. Başkent University Konya Application and Research Center Hospital is a 200-bed hospital with Internal Medicine, Surgery, Gynecology and Pediatrics services, Hemodialysis, Kidney Transplantation unit and Intensive Care units. Patients hospitalized with the diagnosis of pneumonia and positive urine Legionella antigen test (Acro Biotech, USA) were included in the study. The study was conducted retrospectively by scanning patient files. A total of 46 patients were included in the study. 20 patients with nosocomially-acquired Legionella pneumonia (NALP), and 26 patients with community-acquired Legionella pneumonia (CALP) were included in the study. We applied the Centers for Disease Control (CDC) [7] and the World Health Organization (WHO) [8]. criteria for diagnosis both of nosocomial infection and Legionella pneumonia. Demographic information, extrinsic and intrinsic risk factors (Chronic lung disease, cancer, cardiopathies, steroid use, smoking habits, chronic renal failure, diabetes mellitus), clinical, radiological and laboratory findings of the selected patients were recorded. The patients' hemogram, CRP, AST, ALT, LDH, prothrombin time, INR (International Normalized Ratio), total bilirubin, direct bilirubin, sodium potassium, procalcitonin, phosphorus levels and

complete urinalysis were examined. The data were compared statistically. PA chest radiography and/or thorax computed tomography were taken from all patients. Mortality rates, APACHE (Acute Physiology and Chronic Health Evaluation) and SOFA (The Sequential Organ Failure Assessment) scores of the patients were calculated.

Statistical analysis

Collected data were recorded into the previously prepared forms. Statistical analysis was performed using chi-square and independent student t test using SPSS Statistics 25.0 program. Numeric values were reported as mean±standard deviation (SD). p<0.05 was accepted as significant.

Results

Among the risk factors, old age was more common in the NALP group than in the CALP group, whilst chronic lung disease and cancer were more common in the NALP group than in the CALP group. The difference for other risk factors, such as cardiopathies, chronic renal failure, diabetes, smoking habit, and corticosteroid therapy was not statistically significant (Table 1, p>0.05).

Some of the most common clinical manifestations are shown in the table. Statistical analysis showed that myalgia was more common in the CALP group than in the NALP group (p<0.05).

Table 1. Statistical analysis of demographic data and risk factors of 20 NALP and 26 CALP patients

	NALP (n=20)	CALP (n=26)	P value
Age	72±8	67±16	0,01*
Sex (M/F)	13/7	12/14	0,2
Chronic lung disease	11/20	4/26	0,04*
Cancer	3/20	0/26	0,04*
Cardiopathies	2/20	3/26	0,86
Steroid use	1/20	0/26	0.25
Smoking habitis	6/20	6.26	0.59
Chronic renal failure	2/20	3/26	0,9
Diabetes mellitus	6/20	3/26	0.1

*:p<0.05

Table 2. Statistical analysis of demographic data, clinical data of 20 NALP and 26 CALP patients

	NALP (n=20)	CALP (n=26)	P value
Fever	15/20	25/26	0,76
Cough	16/20	22/26	0,68
Sputum	9/20	9/26	0.47
Chest pain	1/20	6/26	0,09
Headache	3/20	3/26	0.73
Confusion	9/20	8/26	0.32
Dyspnea	18/20	21/26	0.39
Abdominal pain	4/20	2/26	0.22
Fatigue	20/20	25/26	0.38
Myalgia	2/20	12/26	0,008*
Anorexia	17/20	23/26	0.73
Diarrhea	1/20	1/26	0.85

*:p<0.05

Table 3. Statistical analysis of laboratory data and Radiological manifestations of 20 NALP and 26 CALP patients

	NALP (n=20)	CALP (n=26)	P value
White blood cell (WBC) /mm ³	12.807±5618	11.920±4761	0.879
CRP, mg/dL	102±79	126±113	0,04*
Hemoglobin, g/dL	13±2	12±2	0.163
Hematocrit, %	41±6	39±6	0.262
Platelet count	179.120±71200	241.807±88457	0.232
ALT, U/L	151±371	35±51	0,007*
AST, U/L	178±452	37±43	0,004*
Total bilirubin, mg/dL	1,4±,3	0.82±0,7	0,037*
Direct bilirubin, mg/dL	1.0±0.9	0.3±0.1	0.001*
Prothrombin time, second	15±9	13±2	0,005*
INR (International Normalized Ratio)	1.4±0.6	1.1±0.2	0.011*
Sodium, mEq/L	132±5	135±3	0.279
Potassium, mEq/L	4.5±0.7	4±0.6	0.663
LDH (Lactate dehydrogenase), U/L	624±702	366±188	0.112
CK (Creatinine kinase), U/L	144±106	649±1188	0.02*
Procalcitonin, ng/mL	7,9±16	7,7±16	0,831
Phosphorus, mg/dL	4.0±2.4	4.0±1.6	0.712
Hematuria	Kas.20	Kas.26	0.393
Right lung infiltration	Eki.20	Kas.26	0.6
Left lung infiltration	Tem.20	Eyl.26	0.98
Bilateral infiltration	Mar.20	Haz.26	0.49
Pleural effusion	Tem.20	Kas.26	0.62
Empyema	Oca.20	0/26	0.25
Mortality rate	25.1±19	18±20	0.97
SOFA	5,5±3,4	4±3.8	0.95
APACHE	14.5±8	10±9	0.87

*:p<0.05

The difference for other common clinical manifestations, such as fever, cough, sputum, chest pain, headache, confusion, dyspnea, abdominal pain, fatigue, anorexia, diarrhea was not statistically significant (Table 2, p>0.05). Laboratory findings of both groups of patients were evaluated. (white blood cell count, CRP, hemoglobin, hematocrit, platelet count, AST, ALT, total bilirubin, direct bilirubin, prothrombin time, INR, sodium, potassium, LDH; CK; procalcitonin, phosphorus, hematuria). While CRP and CK levels were found to be significantly higher in the CALP group than in the NALP group; ALT, AST, total bilirubin, direct bilirubin, prothrombin time, and INR levels were found to be significantly higher in the NALP group compared to the CALP group (Table 3). No significant statistical difference was detected between the two groups in terms of radiological findings (right lung infiltration, left lung infiltration, bilateral infiltration, pleural effusion and empyema) (Table 3). When both groups were compared in terms of mortality rates and SOFA and APACHE scores, no statistically significant difference was detected (Table 3).

Discussion

Clinically, community-acquired pneumonia (CAP) and hospital-acquired pneumonia are very similar and difficult to distinguish. Legionella pneumonia is more common in the elderly. However, CAP can be seen in all age groups [9]. In the first 24-48 hours, weakness, malaise, muscle aches and severe headache occur,

then suddenly rising fever, patchy infiltration in the lung radiogram, dry cough, sometimes side pain, nausea, vomiting and diarrhea are detected as a factor in the atypical pneumonia table. Legionella pneumonia should be considered. Fever above 39-40°C, relative bradycardia, confusion, presence of hyponatremia, extrapulmonary symptoms and unresponsiveness to beta-lactam antibiotic therapy are other clues for Legionella pneumonia [2]. Legionella is a deadly pneumonia agent with a high mortality rate [6]. Unlike classical pneumococcal pneumonia, the symptoms of atypical pneumonia are insidious. Diagnosis is difficult because the clinical, radiological and laboratory findings are not as distinct as those of typical pneumonia, and the causative agents are intracellular microorganisms and do not grow in sputum culture. Diagnosis cannot be made easily because it has nonspecific clinical findings, radiological features, and the need for special laboratory tests [10]. PCR in sputum and bronchoalveolar lavage samples is the preferred diagnostic method in the diagnosis of Legionella pneumonia. PCR has a high diagnostic value and detects all Legionella serogroups [11]. In the diagnosis, an antigen test is performed in the urine, only L. pneumophila shows serogroup 1 and develops due to serogroup 1 in 85% of cases of pneumonia. The sensitivity of this test is 70%, and the specificity is 100 %. It should not be forgotten that Legionella antigen positivity in urine may last more than 300 days and other factors that may cause the current clinic should be excluded in the differential diagnosis [12]. In our study, we diagnosed Legionella with urine antigen, which has high specificity, since we could not access PCR test. Patients with severe immunodeficiency and oncological/ hematological malignancies are particularly at risk for the development of Legionella infection and the serious prognosis of the disease. Other malignancies, diabetes mellitus, chronic lung disease, smoking, old age (over 50 years of age) and male gender are also among the risk factors [13]. Determining risk factors is important in this sense, as the clinical course varies depending on the patient's immune system, the presence of additional diseases, early treatment at the appropriate time and whether complications develop [14]. In our study, it was found that there was a difference in these risk factors between the NALP and CALP groups. In the NALP group, advanced age, malignancy and chronic lung disease frequency were determined as risk factors compared to the CALP group. LD has a wide clinical spectrum that can range from mild cough, and fever to coma and affects many systems. It has been reported that the incubation period is 2-10 days, although the period is generally short in immunosuppressed people and can extend up to 20 days. The disease first begins with nonspecific findings such as fever, malaise, myalgia, headache, and nonproductive cough [6]. The most common clinical findings in our patients were fever, cough, shortness of breath, loss of appetite, fatigue, muscle pain, and chest pain and no difference was detected between the two groups in terms of symptoms other than myalgia. Myalgia was significantly higher in the CALP group. Diarrhea is a frequently observed gastrointestinal system symptom and is seen in 25-50% of cases [6]. Diarrhea complaints were less frequent on average in our cases and no

statistically significant difference was detected between the two groups. In another study comparing the CALP and NALP groups, cough, chest pain, neurological symptoms (headache, confusion), and gastrointestinal symptoms (nausea, vomiting, diarrhea) were found to be significantly higher in the NALP group [15].

Studies have shown that LD most often appears as an airspace consolidation involving one of the lower lobes on lung radiographs, while pleural effusion and mediastinal lymphadenopathy are less common [5, 16].

It has also been suggested that the resolution of pulmonary infiltrates on chest radiographs takes longer than pneumonia caused by other pathogens [17]. In a more recent study, Poirier et al. showed that the early radiographic and tomographic signs of LD were similar to those found in community-acquired pneumonia of other bacterial origin [16]. In our study, when the chest radiographs of the patients were evaluated, it was seen that there was infiltration in all patients. When the regions where infiltrations were observed between the two groups were compared, no significant difference was detected between the groups. In the study conducted by Pedro-Botet et al., similar to our findings, no difference was detected between the two groups in terms of radiological findings [15].

In laboratory tests for Legionella pneumonia, elevated transaminases, creatinine phosphokinase and LDH, hyponatremia and hypophosphatemia may be observed [18]. In our study, CRP, AST, ALT, Prothrombin time and total bilirubin values were found to be higher in the NALP group. In the study conducted by Pedro-Botet et al., ALT elevation was found to be statistically significant in the NALP group [15].

Legionnaires' disease ranges from mild to severe. In a case series of 214 patients hospitalized for Legionnaires' disease, 47 percent had moderate/severe pneumonia (Pneumonia Severity Index IV to V) and 18 percent required intensive care unit (ICU) admission [19]. In other case series, 44 percent required ICU admission. Even in tertiary care centers, the mortality rate ranges from approximately 1 to 10 percent [19-21]. After ICU admission, mortality can be over 30 percent and some patients require extracorporeal membrane oxygenation [22]. In a recent study in which 50 patients were included in the study, the mortality rate was found to be 73% in cases in which 26% were diagnosed with hospital-acquired LD, and the SOFA score was found to be high in hospital-acquired cases [23]. However, in our study, we did not detect a statistically significant difference in mortality rates, SOFA and APACHE scores between the NALP and CALP groups.

As a result, since *L. pneumophila* pneumonia can progress with severe complications such as ARDS, tests for early diagnosis should be requested and treatment should be started without delay in cases where Legionella pneumonia is suspected based on anamnesis, clinical and laboratory findings. *L. pneumophila* can be both community and hospital acquired. In this study, we concluded that there may be differences in laboratory, clinical, risk factors and radiological imaging between community- and hospital-acquired Legionella pneumonia. We think that randomized, more comprehensive studies should be conducted to investigate the differences between community-acquired and hospital-acquired Legionella pneumonia.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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